STN-Structure Search 11.7.05

10/524,819

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L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1049862 CAPLUS
DOCUMENT NUMBER: 143:347066
TITLE: Preparation of heterocyclic substituted hydroxyphenyl phenanthridines as PDE4 inhibitors
INVENTOR(S): Schmidt, Beate; Flockerzi, Dieter; Hatzelmann, Armin; Zitt, Christof; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Kautz, Ulrich
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005090311	A1	20050929	WO 2005-EP50946	20050303

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

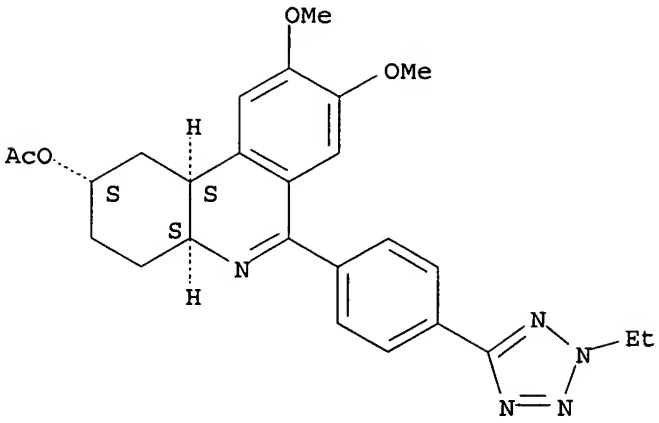
PRIORITY APPLN. INFO.: EP 2004-5005 A 20040303
EP 2004-106372 A 20041207

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = OH, alkoxy, cycloalkoxy, etc.; R2 = OH, cycloalkylmethoxy, 2,2-difluoroethoxy, etc. or R1 and R2 together are alkylenedioxy group; R3 and R6 independently = H or alkyl; R4 = OR9; R9 = H, alkyl, alkoxyalkyl, etc.; R5 = H or alkyl; R7 = H, halo, alkoxy, etc.; R8 = (un)substituted, (un)saturated heterocycle] and their pharmaceutically acceptable salts, were prepared and disclosed as inhibitors of PDE4. Thus, e.g., II was prepared by cyclization of acetic acid (1RS,3RS,4RS)-4-{[1-(4-imidazol-1-yl-phenyl)methanoyl]amino}-3-(3-ethoxy-4-methoxyphenyl)cyclohexyl ester (preparation given) with phosphorous pentachloride followed by reduction of the ester to the resp. alc. The inhibitory activity of I towards PDE4 was evaluated using scintillation proximity assay and it was revealed that selected compds. of the invention possessed -log IC50 values in the range of 7.43 up to 9.92 mol/L. I as inhibitors of PDE4 should prove useful in the treatment of respiratory disorders. Pharmaceutical compns. comprising I are disclosed.

IT **865475-11-2P 865475-13-4P 865475-14-5P**
865475-15-6P 865475-17-8P 865475-18-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic substituted hydroxyphenyl phenanthridines as PDE4 inhibitors)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1026938 CAPLUS
DOCUMENT NUMBER: 143:326233
TITLE: Preparation of amido-substituted phenylphenanthridines as PDE4 inhibitors for the treatment of respiratory diseases
INVENTOR(S): Schmidt, Beate; Kautz, Ulrich
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087745	A1	20050922	WO 2005-EP51054	20050309

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2004-100990 A 20040310
EP 2004-106677 A 20041217

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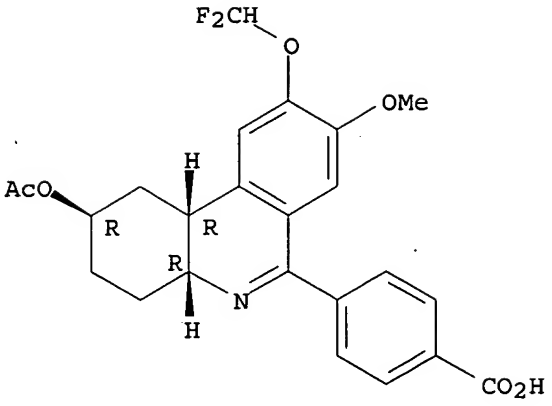
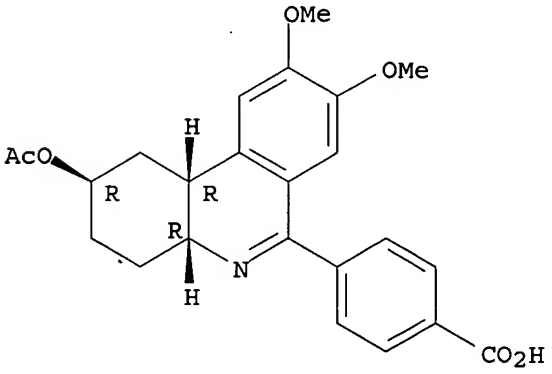


RN 669001-66-5 CAPLUS
CN Benzoic acid, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1026937 CAPLUS
DOCUMENT NUMBER: 143:347065
TITLE: Preparation of thio-containing phenylphenanthridines as PDE4 inhibitors for the treatment of respiratory diseases
INVENTOR(S): Schmidt, Beate; Flockerzi, Dieter; Hatzelmann, Armin; Zitt, Christof; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Kautz, Ulrich
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087744	A1	20050922	WO 2005-EP51052	20050309
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2004-100988 A 20040310
EP 2005-100692 A 20050201

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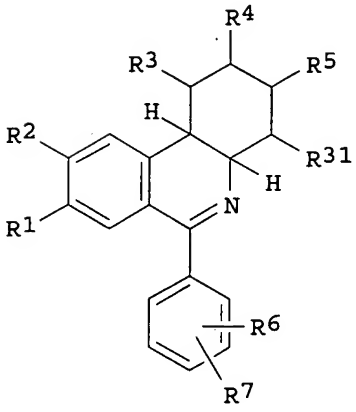

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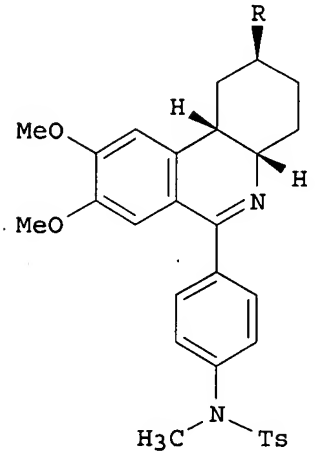


II

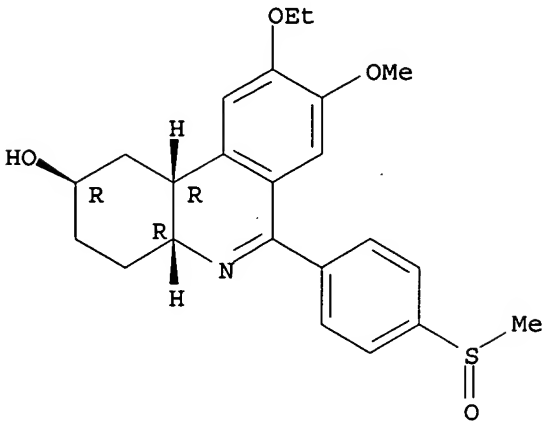
AB Title compds. I [wherein R1, R2 = OH or (cyclo)alkoxy; R3, R31 = H or alkyl; R4 = OH, alkoxy or alkylcarbonyloxy; R5 = H or alkyl; R6 = H, halo, alkyl or alkoxy; R7 = (un)substituted SO2NH2; etc., or their salts and the N-oxides, and the salts of the N-oxides] were prepared as PDE4 inhibitors. For instance, II (R = OH) was synthesized by hydrolysis of its ester II (R = OAc) with Cs2CO3 in methanol. Representative I, including II (R = OH), were found to inhibit PDE4B2 with pIC50 values of 7.52 - 10.06. Therefore, I and pharmaceutical compns. thereof are useful for treating PDE-mediated disorders, such as respiratory diseases.

IT **865291-76-5P 865291-77-6P 865291-78-7P**
865291-79-8P 865291-81-2P 865291-82-3P
865291-83-4P 865291-84-5P 865291-85-6P
865291-86-7P 865291-87-8P 865292-08-6P
865292-09-7P 865292-10-0P 865292-11-1P
865292-13-3P 865292-14-4P 865292-15-5P
865292-16-6P 865292-17-7P 865292-18-8P
865292-19-9P 865292-20-2P 865292-21-3P
865292-22-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibitor; preparation of thio-containing phenylphenanthridines as PDE4 inhibitors for treatment of respiratory diseases)

RN 865291-76-5 CAPLUS

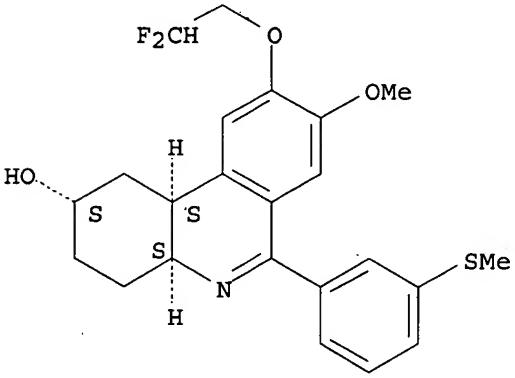
CN Benzenesulfonamide, N-[4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]phenyl]-4-methyl-, rel- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



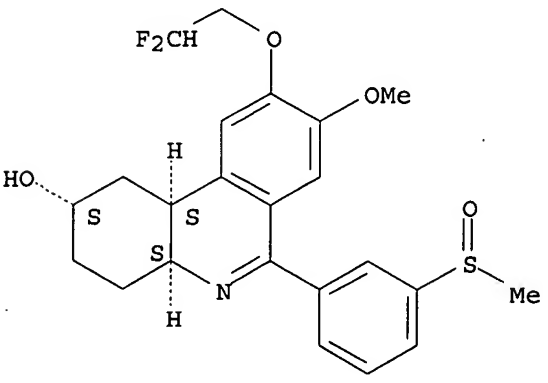
RN 865292-34-8 CAPLUS
CN 2-Phenanthridinol, 9-(2,2-difluoroethoxy)-1,2,3,4,4a,10b-hexahydro-8-methoxy-6-[3-(methylthio)phenyl]-, (2R,4aR,10bR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 865292-35-9 CAPLUS
CN 2-Phenanthridinol, 9-(2,2-difluoroethoxy)-1,2,3,4,4a,10b-hexahydro-8-methoxy-6-[3-(methylsulfinyl)phenyl]-, (2R,4aR,10bR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1004712 CAPLUS
DOCUMENT NUMBER: 143:306199
TITLE: Preparation of difluoroethoxy-substituted hydroxy-6-phenylphenanthridines as PDE4 inhibitors
INVENTOR(S): Schmidt, Beate; Flockerzi, Dieter; Hatzelmann, Armin; Zitt, Christof; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Kautz, Ulrich
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085203	A1	20050915	WO 2005-EP51022	20050308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2004-100989 A 20040310
EP 2005-100539 A 20050127

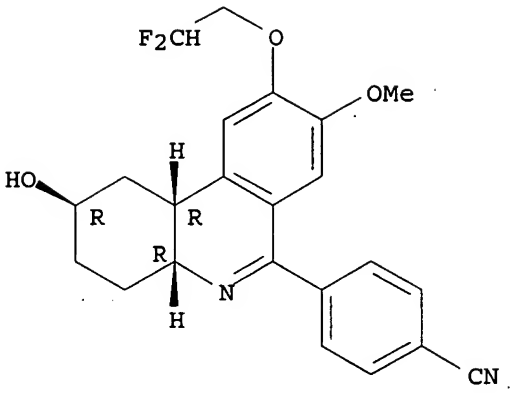
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [when R1 = independently OH and F-substituted/cyclo/alkoxy, 2,2-difluoroethoxy, etc., R2 = 2,2,-difluoroethoxy; when R1 = 2,2,-difluoroethoxy, R2 = independently OH and F-substituted/cyclo/alkoxy, 2,2-difluoroethoxy, etc.; R3, R31 = independently H, alkyl; R4 = H, alkyl, OR41; R5 = OR51; R41, R51 = independently H, alkoxy/hydroxy/F-substituted/alkyl, alkylcarbonyl; R6 = H, alkyl, CF3, halo, alkoxy, etc.; R7 = H, alkyl, OH, halo, etc.; their salts, N-oxides, and the salts of the N-oxides] were prepared as effective PDE4 inhibitors for treating respiratory diseases. Thus, rac-II was prepared in 9 steps from isovanillin and 2-bromo-1,1-difluoroethane (not all intermediates isolated). Rac-II inhibited PDE4 with -log IC50 = 9.15 mol/l.

IT **864711-33-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of difluoroethoxy-substituted hydroxy-6-phenylphenanthridine as PDE4 inhibitors)

RN 864711-33-1 CAPLUS
CN 2-Phenanthridinol, 9-(2,2-difluoroethoxy)-6-(4-fluorophenyl)-



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1001807 CAPLUS
DOCUMENT NUMBER: 143:306198
TITLE: Preparation of 2- or 3-hydroxy-6-(substituted-carbonylaminophenyl)phenanthridines as PDE4 inhibitors
INVENTOR(S): Schmidt, Beate; Flockerzi, Dieter; Hatzelmann, Armin; Zitt, Christof; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Kautz, Ulrich
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005084104	A2	20050915	WO 2005-EP51025	20050308
WO 2005084104	A3	20051013		

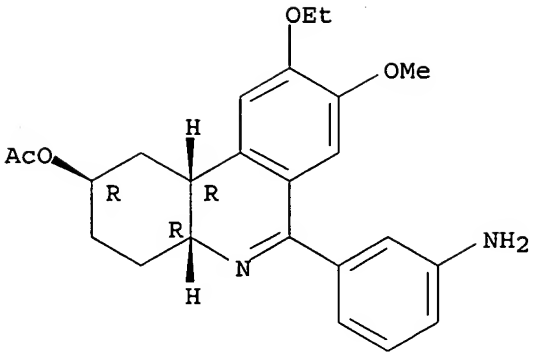
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2004-100959 A 20040309
EP 2005-100545 A 20050127

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1, R2 = independently OH and F-substituted/cyclo/alkoxy, 2,2-difluoroethoxy, etc.; R1-R2 = alkylenedioxy; R3, R31 = independently H, alkyl; R4 = H, alkyl, OR41; R5 = OR51; R41, R51 = independently H,



L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:902858 CAPLUS
DOCUMENT NUMBER: 143:248297
TITLE: Preparation of guanidinyl hydroxyphenylphenanthridines as PDE4 inhibitors
INVENTOR(S): Schmidt, Beate; Flockerzi, Dieter; Hatzelmann, Armin; Zitt, Christof; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Kautz, Ulrich
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

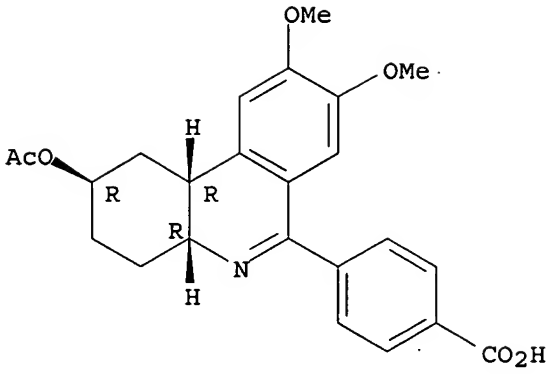
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077906	A1	20050825	WO 2005-EP50708	20050217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2004-3592 A 20040218
GI

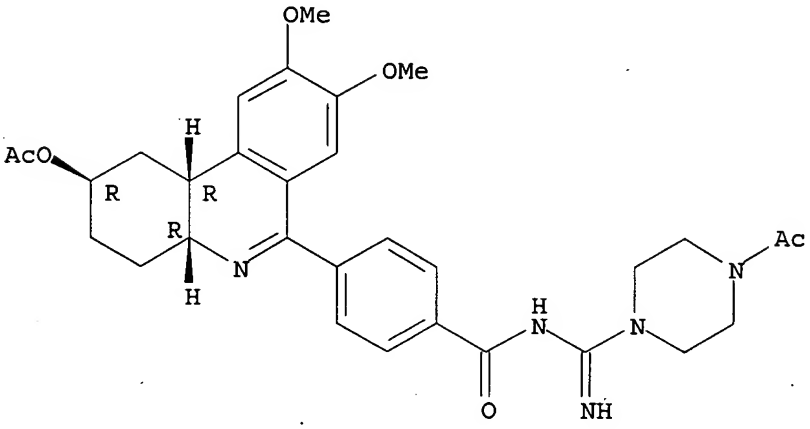
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = OH, alkoxy, cycloalkoxy, etc.; R2 = OH, cycloalkylmethoxy, cycloalkoxy, etc. or R1 and R2 together form alkylenedioxy group; R3 = H or alkyl; R4 = OR9 and R5 = H or alkyl or R4 = H or alkyl and R5 = OR9; R6 = H or alkyl; R7 = (un)substituted guanidinyl; R8 = H, halo, nitro, etc.; R9 = H, alkyl, alkoxyalkyl, etc.] and their pharmaceutically acceptable salts, are prepared and disclosed as phosphodiesterase 4 (PDE4) inhibitors. Thus, e.g., II was prepared by coupling of 4-((2RS,4aRS,10bRS)-2-acetoxy-8,9-dimethoxy-1,2,3,4,4a,10b-



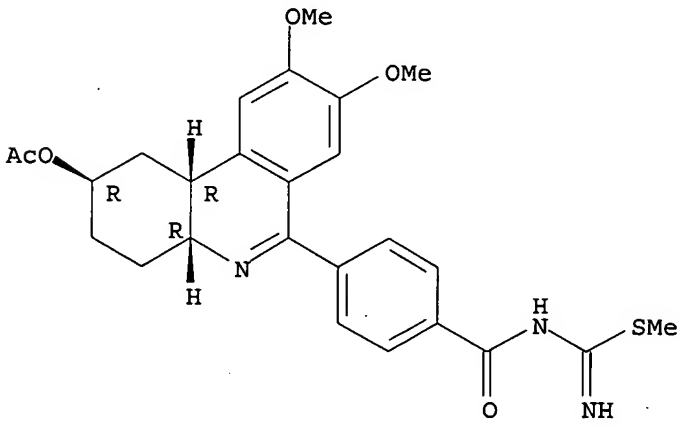
RN 862993-78-0 CAPLUS
CN Benzamide, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[(4-acetyl-1-piperazinyl)iminomethyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 862993-79-1 CAPLUS
CN Carbamimidothioic acid, [4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]benzoyl]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

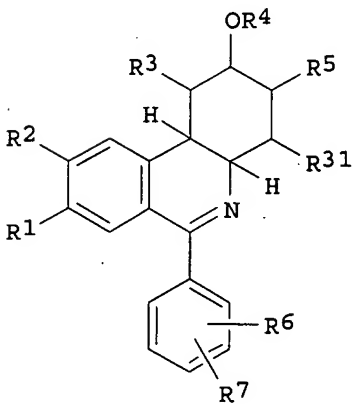


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

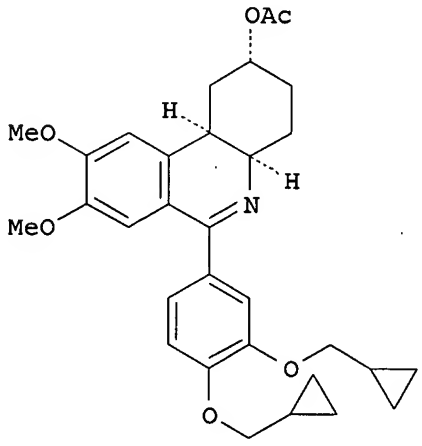
L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:203669 CAPLUS
DOCUMENT NUMBER: 140:235615
TITLE: Preparation of 2-Hydroxy-6-phenylphenanthridines as PDE-4 inhibitors
INVENTOR(S): Kautz, Ulrich; Schmidt, Beate
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004019944	A1	20040311	WO 2003-EP9547		20030828
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW					
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
CA 2495827	AA	20040311	CA 2003-2495827		20030828
EP 1539164	A1	20050615	EP 2003-790931		20030828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005239817	A1	20051027	US 2005-524819		20050218
PRIORITY APPLN. INFO.:			EP 2002-19335	A	20020829
			WO 2003-EP9547	W	20030828

OTHER SOURCE(S): MARPAT 140:235615
GI



I



II

AB The title compds. I [wherein R1 and R2 = independently OH, alkoxy, cycloalkyloxy, cycloalkylmethoxy, or fluorinated alkoxy; or R1 and R2 together form alkylenedioxy; R3 = H or alkyl; R31 = H or alkyl; R4 = H, alkyl, fluorinated alkyl, alkoxyalkyl, hydroxyalkyl, or alkylcarbonyl; R5

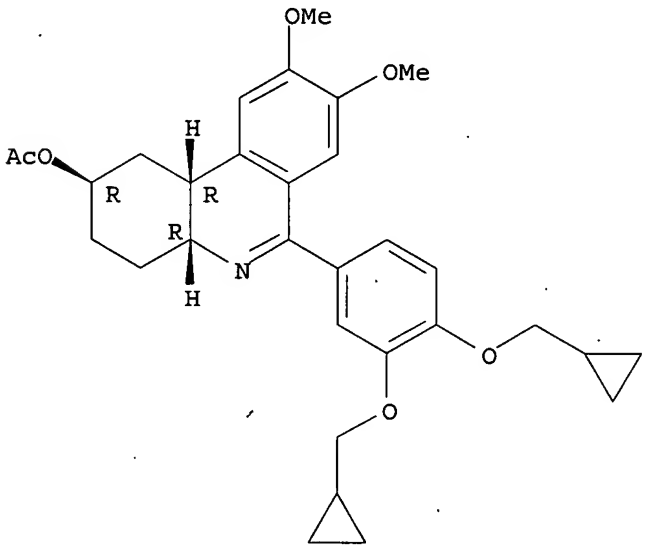
= H or alkyl; R6 = H, alkyl, CF3, alkoxy, fluorinated alkoxy, cycloalkyloxy, cycloalkylmethoxy, H, NO2, CN, OH, alkylcarbonyloxy, NH2, alkylamino, dialkylamino, Ph, Ph-alkyl, alkylcarbonylamino, PhO, or (un)substituted CO2H; R7 = H, alkyl, OH, halo, alkoxy, fluorinated alkoxy, cycloalkyloxy, cycloalkylmethoxy, or (un)substituted CO2H] or salts, N-oxides, or salts of the N-oxides thereof are prepared as phosphodiesterase (PDE) 4 inhibitors. For example, the compound II was prepared in a multi-step synthesis. I showed inhibitory activity with "-logIC50" of 7.09 to 9.74 against human PDE4. I are useful for the treatment of respiratory disorders or dermatosis (no data).

IT **669000-55-9P 669000-56-0P 669000-60-6P 669000-61-7P 669000-66-2P 669000-68-4P 669000-96-8P 669001-26-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of phenanthridine derivs. as PDE-4 inhibitors)

RN 669000-55-9 CAPLUS

CN 2-Phenanthridinol, 6-[3,4-bis(cyclopropylmethoxy)phenyl]-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-, acetate (ester), (2R,4aR,10bR)-rel- (9CI) (CA INDEX NAME)

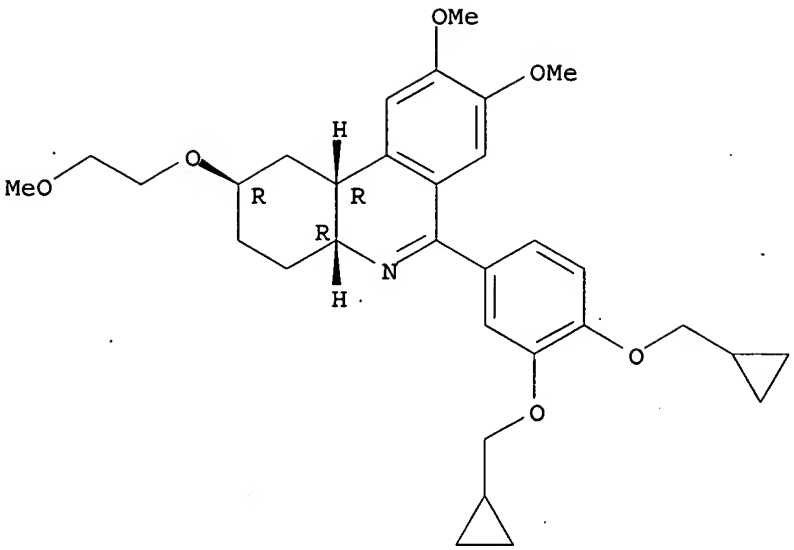
Relative stereochemistry.



RN 669000-56-0 CAPLUS

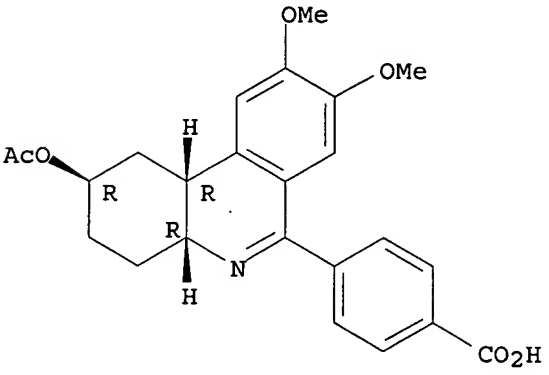
CN Benzoic acid, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 669001-66-5 CAPLUS
CN Benzoic acid, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



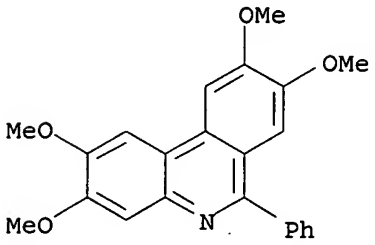
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1946:5229 CAPLUS
DOCUMENT NUMBER: 40:5229
ORIGINAL REFERENCE NO.: 40:876a-i
TITLE: Phenanthridine series. I. Cyclization of 2-formamidobiphenyls
AUTHOR(S): Ritchie, E.
CORPORATE SOURCE: Univ. of Sydney, Australia
SOURCE: Journal and Proceedings of the Royal Society of New South Wales (1945), 78, 134-40
CODEN: JPRSA5; ISSN: 0035-9173
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A solution of 56 g. o-(MeO)2C6H4 in 150 cc. EtOH was stirred and treated alternately with 100 g. iodine and 60 g. HgO during 3 h. After 1 h. the mixture was filtered and the EtOH was distilled from the filtrate. The residue was dissolved in Et2O, washed with Na2S2O3, NaOH, and H2O. After drying,

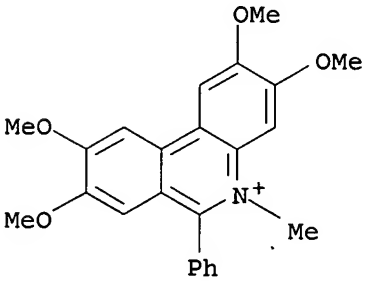
the Et2O was removed and the residue distilled to give 60 g. 4-iodoveratrole (I), b26 163-4°. Heating of 25 g. I and 25 g. Cu powder in CO2 at 235° for 1 h., cooling, extraction with MeOH, and evaporation of the MeOH gave 10 g. 3,3',4,4'-tetramethoxybiphenyl (II), m. 133° (MeOH). II (5.5 g.) in 60 cc. AcOH at room temperature was treated with 1.2 g. HNO3 in 3 cc. AcOH during 15 min. After 30 min., the mixture was warmed on the H2O bath 15 min., cooled, and diluted with ice-H2O. The precipitate was recrystd. from EtOH to give 5 g. 2-nitro-4,4',5,5'-tetramethoxybiphenyl (III), yellow rhombs, m. 149°. Nitration of II or III in AcOH with HNO3 yielded 2,2'-dinitro-4,4',5,5'-tetramethoxybiphenyl (IV), fine yellow needles, m. 218° (EtOH). Hydrogenation of 5 g. III in 200 cc. hot EtOH at ordinary pressure in the presence of Raney Ni yielded 100% 2-amino-4,4',5,5'-tetramethoxybiphenyl (V), colorless prisms from C6H6, m. 151°; piperonylidene derivative, from V and piperonal, yellow plates from EtOH, m. 155°; salicylidene derivative, orange needles from EtOH, m. 144°. Acetylating of V with Ac2O yielded 2-acetamido-4,4',5,5'-tetramethoxybiphenyl (VI), colorless prisms from aqueous EtOH, m. 164°. Similarly (EtCO)2O yielded 2-propionamido-4,4',5,5'-tetramethoxybiphenyl (VII), colorless plates from EtOH, m. 138°, and BzCl in pyridine gave 2-benzamido-4,4',5,5'-tetramethoxybiphenyl (VIII), colorless needles from aqueous EtOH, m. 128°. VI (4 g.) was warmed with 10 cc. POCl3 under reflux 1 h. and the excess POCl3 was removed. The residue was warmed with dilute NaOH, and the precipitate recrystd. from C6H6 to give 85% 6-methyl-2,3,8,9-tetramethoxyphenanthridine (IX), colorless rods, m. 212°; methiodide, from IX and MeI 2 h. at 100°, yellow needles, m. 260-84° (decomposition). In like manner VII yielded 85% 6-ethyl-2,3,8,9-tetramethoxyphenanthridine, colorless prisms, m. 202° (methiodide, yellow needles from dilute EtOH, m. 286° (decomposition)), and VIII yielded 90% 6-phenyl-2,3,8,9-tetramethoxyphenanthridine, colorless blades, m. 207° (methiodide, yellow needles from dilute EtOH, 273° (decomposition)). A mixture of 10 g. IX, 50 cc. EtOH, and 20 cc. 40% HCHO was refluxed 3 h., and then 20 cc. HCHO was added. After refluxing for another 10 h., 10 cc. HCHO was added, refluxing was continued 3 h., and all solvent was evaporated The residue was diluted with H2O, treated with excess NH4OH, boiled, and cooled. The precipitate, upon recrystn. from C6H6 and C6H6-EtOH, gave 6.5 g. 6-(2,2'-dihydroxyisopropyl)-2,3,8,9-tetramethoxyphenanthridine (X), colorless prisms, m. 214°. X (4.5 g.), 50 cc. H2O, and 1.2 cc. H2SO4 were heated on the H2O bath and treated with a solution of 7.5 g. K2Cr2O7 and 5.6 cc. H2SO4 in 35 cc. H2O during 30 min. After 3 h. the mixture was cooled and diluted, and the precipitate was purified by dissolving in NaOH and repptg. with AcOH to give 3.9 g. 2,3,8,9-tetramethoxy-6-phenanthridinecarboxylic acid, decomposing 240°, which rapidly decarboxylated when maintained at 245° to yield 2.5 g. 2,3,8,9-tetramethoxyphenanthridine as colorless needles from MeOH, m. 185° (after partially m. 135° and resolidifying); methiodide (XI), pale yellow needles from aqueous EtOH, m. 295°. V (2 g.) and 15 cc. HCO2H were refluxed 3 h., cooled, and diluted The precipitate was recrystd. from aqueous EtOH to give 1.7 g. 2-formamido-4,4',5,5'-tetramethoxybiphenyl (XlI), colorless plates, m. 168°. Boiling XII with POCl3 gave only tar, and reactions at lower temps. or in a solvent gave either a tar or no reaction. Cyclization of 7.5 g. XII by boiling with 10 g. P2O5 in 80 cc. C6H4Me2, followed by methylating with excess MeI at 100°, yielded 0.3 g. XI. The phenanthridine derivs. prepared above all show marked blue fluorescence in neutral solution and stronger fluorescence in AcOH. The yellow methiodides are strongly fluorescent in aqueous EtOH.

IT **861002-27-9**, Phenanthridine, 2,3,8,9-tetramethoxy-6-phenyl-
861003-42-1, Phenanthridinium, 2,3,8,9-tetramethoxy-5-methyl-6-phenyl-, iodide
(preparation of)

RN 861002-27-9 CAPLUS
CN Phenanthridine, 2,3,8,9-tetramethoxy-6-phenyl- (4CI) (CA INDEX NAME)



RN 861003-42-1 CAPLUS
CN Phenanthridinium, 2,3,8,9-tetramethoxy-5-methyl-6-phenyl-, iodide (4CI) (CA INDEX NAME)



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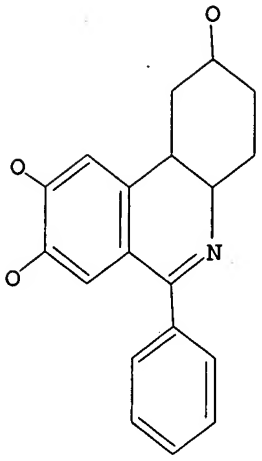
L3 309 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:42:04 ON 07 NOV 2005
L4 8 S L3

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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